

AMENDMENTS TO THE CLAIMS

1. **(Original)** A method of making an antibody molecule, the antibody containing an immunoglobulin heavy chain comprising a $\alpha 3$ domain or a mu domain, the method comprising:

- (a) Providing a nucleotide sequence encoding the immunoglobulin heavy chain;
- (b) Modifying the nucleotide sequence in the region of the nucleotide sequence encoding the C-terminus 18 amino acids of the completed heavy chain to remove, or reduce the effectiveness of, one or more vacuolar targeting signal sequences to form a modified nucleotide sequence;
- (c) Inserting the modified nucleotide sequence into a host cell; and
- (d) Causing the host cell to express the modified nucleotide sequence to form the modified antibody heavy chain and secrete the modified antibody heavy chain from the host cell.

2-33. Cancelled

34. **(Previously presented)** A method according to claim 1 wherein the heavy chain molecule is IgA, IgM or an IgA/G hybrid.

35. **(Previously presented)** A method according to claim 1 wherein nucleotide sequence is modified by one or more point mutations of the nucleotide sequence, deleting one or more nucleotides, adding one or more nucleotides and/or replacing one or more nucleotides with a synthetic nucleotide sequence.

36. **(Currently amended)** A method according to claim 35, wherein the synthetic nucleotide sequence encodes an amino acid sequence of general formula:



where: C = a cysteine residue

Xaa₁ = independently any amino acid with the proviso that it is not from

I, L or forms a consecutive sequence X₁ X₂ X₃ V S X₄ (SEQ ID NO: 1)

where: X₁ = N, H or L

X₂ = V or Y

X₃ = S or N

X₄ = aliphatic amino acid

Xaa₂ = independently any amino acid

m = at least 2

n = 0 to 5.

37. **(Previously presented)** A method according to claim 36, wherein Xaa₂ is Y and n = 1.

38. **(Previously presented)** A method according claim 1, wherein nucleotides encoding the last 16 amino acids of the heavy chain are deleted.

39. **(Previously presented)** A method according to claim 1 wherein the resultant amino acid sequence at the C terminus of the heavy chain has a formula selected from:

(a) SCMVGHEALPMNFTQKTIDRLSGKPACY (SEQ ID NO: 7),

(b) SCMVGHEALPMNFTQKTIDRLSGKPAAACY (SEQ ID NO: 8),

(c) SCMVGHEALPMNFTQKTIDRLSGKPHASTPEPDPVACY (SEQ ID NO: 9) and

(d) SCMVGHEALPMNFTQKTIDRLSGKPAAAAACY (SEQ ID NO: 69)

40. **(Currently amended)** A method according to claim 1 wherein the nucleotide sequence modified originally encoded the amino acid sequence:

X₁ X₂ X₃ V S X₄ (SEQ ID NO: 1)

where: X₁ = N, H or L

X₂ = V or Y

X₃ = S or N

X₄ = aliphatic amino acid.

41. **(Previously presented)** A method according to claim 40, wherein the amino acid sequence is: N V S V S V (SEQ ID NO: 2).

42. **(Previously presented)** A method according to claim 1 wherein the nucleotide sequence modified encoded L or I.

43. **(Previously presented)** A method according to claim 42, wherein the modified amino acid is one or both of an isoleucine 3 amino acids and/or 10 amino acids from the C-terminus end of the completed heavy chain.

44. **(Previously presented)** A method according to claim 1, wherein the nucleotide sequence modified is within the sequence:

P T X₁ X₂ X₃ V S X₄ X₅ X₆ X₇ X₈ X₉ X₁₀ X₁₁ X₁₂ C X₁₃ (SEQ ID NO: 5)

where: X₁ = N, H or L, preferably N

X₂ = V or Y, preferably V

X₃ = S or N

X₄ = an aliphatic amino acid, preferably V or L

X₅ = an aliphatic amino acid, preferably I, V or L

X₆ = M, V or L, especially M

X₇ = S or A

X₈ = E or D

X₉ = any amino acid, preferably G, V, A or T

X₁₀ = D, E, G or A, preferably D

X₁₁ = G or S, preferably G

X₁₂ = I, T, V, Z or A, preferably I or T

X₁₃ = may or may not be present and, where present is A or Y

45. **(Currently amended)** A method of adding J-chain binding capability to the heavy chain of an antibody comprising the steps of:

(a) providing a nucleotide encoding an immunoglobulin heavy chain;

(b) adding to that nucleotide a nucleotide sequence encoding a synthetic tail with the amino acid sequence:

-(Xaa₁)_m C(Xaa₂)_n

where: C = Cys

Xaa₁ is independently any amino acid with the proviso that it is not I or L or forms a consecutive sequence X₁ X₂ X₃ V S X₄ (SEQ ID NO: 1) (where X₁ = N, H or L; X₂ =

V or Y; X₃ = S or N; X₄ = aliphatic amino acid)

Xaa₂ = independently any amino acid

m = at least 2

n = 0 to 5; and

(c) expressing the completed nucleotide in a host cell to form an immunoglobulin heavy chain capable of binding J-chain.

46. **(Previously presented)** A method according to claim 1 wherein the host cell is a plant cell.

47. **(Previously presented)** A method according to claim 45 wherein the host cell is a plant cell.

48. **(Previously presented)** A method according to claim 46, wherein the plant cell is part of a transgenic plant.

49. **(Previously presented)** A method according to claim 47, wherein the plant cell is part of a transgenic plant.

50. **(Previously presented)** A method according to claim 1 additionally comprising the step of isolating and purifying the antibody molecule.

51. **(Previously presented)** A method according to claim 45 additionally comprising the step of isolating and purifying the antibody molecule.

52. **(Previously presented)** A method according to claim 50, wherein the antibody is subjected to a protease digest to for Fab or F(ab')₂ fragments.

53. **(Previously presented)** A method according to claim 51, wherein the antibody is subjected to a protease digest to for Fab or F(ab')₂ fragments.

54. **(Previously presented)** An antibody containing a heavy chain comprising an $\alpha 3$ domain or a mu domain, the $\alpha 3$ domain or mu domain lacking one or more targeting signals towards the C-terminal end.

55. **(Currently Amended)** An antibody capable of binding J-chain comprising at its C-terminal end the sequence:

-(Xaa₁)_m C(Xaa₂)_n

where: C = Cys

Xaa₁ is independently any amino acid with the proviso that it is not I or L or forms a consecutive sequence X₁ X₂ X₃ V S X₄ (SEQ ID NO: 1) (where X₁ = N, or L; X₂ = V or Y; X₃ = S or N; X₄ = aliphatic amino acid)

Xaa₂ = independently any amino acid

m = at least 2

n = 0 to 5

56. **(Currently Amended)** An antibody according to claim 54 which does not contain the targeting signal: X₁ X₂ X₃ V S X₄ (SEQ ID NO: 1)

where: X₁ = N, H or L

X₂ = V or Y

X₃ = S or N

X₄ = aliphatic amino acid.

57. **(Currently Amended)** An antibody according to claim 55 which does not contain the targeting signal: X₁ X₂ X₃ V S X₄ (SEQ ID NO: 1)

where: X₁ = N, H or L

X₂ = V or Y

X₃ = S or N

X₄ = aliphatic amino acid.

58. **(Previously presented)** An antibody according to claim 56, wherein the targeting signal is N V S V S V (SEQ ID NO: 2).

59. **(Previously presented)** An antibody according to claim 57, wherein the targeting signal is N V S V S V (SEQ ID NO: 2).

60. **(Previously presented)** An antibody according to claim 54 which contains one or no isoleucine or leucine amino acids within the last 18 amino acids at the C-terminus of the heavy chain of the antibody.

61. **(Previously presented)** An antibody according to claim 55 which contains one or no isoleucine or leucine amino acids within the last 18 amino acids at the C-terminus of the heavy chain of the antibody.

62. **(Currently amended)** An antibody according to claim 54 comprising at the C-terminus end of the heavy chain of antibody, the sequence:

$-(Xaa_1)_m C(Xaa_2)_n$

where: C = cysteine residue

Xaa₁ = independently any amino acid with the proviso that it is not I or L
or forms a consecutive sequence X₁ X₂ X₃ V S X₄ (SEQ ID NO: 2)

where: X₁ = N, H or L

X₂ = V or Y

X₃ = S or N

X₄ = aliphatic amino acid

Xaa₂ = independently any amino acid

m = at least 2

n = 0 to 5.

63. **(Currently amended)** An antibody according to claim 55 comprising at the C-terminus end of the heavy chain of antibody, the sequence:

$-(Xaa_1)_m C(Xaa_2)_n$

where: C = cysteine residue

Xaa₁ = independently any amino acid with the proviso that it is not I or L
or forms a consecutive sequence X₁ X₂ X₃ V S X₄ (SEQ ID NO: 2)

where: X₁ = N, H or L

X₂ = V or Y

X₃ = S or N

X₄ = aliphatic amino acid

Xaa₂ = independently any amino acid

m = at least 2

n = 0 to 5.

64. **(Previously presented)** An antibody according to claim 54 in which at least two, preferably two to four, glycine or alanine residues are present downstream of a C-terminal targeting sequence

65. **(Previously presented)** An antibody according to claim 55 in which at least two, preferably two to four, glycine or alanine residues are present downstream of a C-terminal targeting sequence

66. **(Previously presented)** An antibody according to claim 54 in which at least the terminal amino acid residue of a C-terminal targeting sequence is replaced by at least two, preferably two to four, glycine or alanine residues.

67. **(Previously presented)** An antibody according to claim 55 in which at least the terminal amino acid residue of a C-terminal targeting sequence is replaced by at least two, preferably two to four, glycine or alanine residues.

68. **(Previously presented)** A method of treating a disease by administering an antibody according to claim 54 to a patient.

69. **(Previously presented)** A method of treating a disease by administering an antibody according to claim 55 to a patient.

70. **(Previously presented)** A method of prophylaxis, comprising administering an antibody according to claim 54 to a person or animal.

71. **(Previously presented)** A method of prophylaxis, comprising administering an antibody according to claim 55 to a person or animal.

72. **(Previously presented)** A vector comprising a nucleotide sequence encoding an antibody according to claim 54.

73. **(Previously presented)** A vector comprising a nucleotide sequence encoding an antibody according to claim 55.

74. **(Previously presented)** A host cell comprising a nucleotide sequence encoding antibody according to claim 54.

75. **(Previously presented)** A host cell comprising a nucleotide sequence encoding antibody according to claim 55.

76. **(Previously presented)** A host cell comprising a vector according to claim 72.

77. **(Previously presented)** A host cell comprising a vector according to claim 73.

78. **(Previously presented)** A transgenic plant comprising a nucleotide encoding an antibody according to claim 54.

79. **(Previously presented)** A transgenic plant comprising a nucleotide encoding an antibody according to claim 55.

80. **(Previously presented)** An immunoassay comprising an antibody as defined in claim 54.

81. **(Previously presented)** An immunoassay comprising an antibody as defined in claim 55.

82. **(New)** The method of claim 1, further comprising adding to the nucleotide sequence encoding the immunoglobulin heavy chain a nucleotide sequence encoding a synthetic tail with the amino acid sequence $-(Xaa_1)_m C(Xaa_2)_n$, wherein:

- C = Cys
- Xaa₁ is independently any amino acid with the proviso that it is not I or L or forms a consecutive sequence X₁ X₂ X₃ V S X₄ (where X₁ = N, H or L; X₂ = V or Y; X₃ = S or N; X₄ = aliphatic amino acid)
- Xaa₂ = independently any amino acid
- m = at least 2
- n = 0 to 5; and

wherein said synthetic tail adds J-chain binding capability to the heavy chain of the antibody.

83. **(New)** A method according to claim 82 wherein the host cell is a plant cell.

84. (New) A method according to claim 83, wherein the plant cell is part of a transgenic plant.

85. (New) A method according to claim 82 additionally comprising the step of isolating and purifying the antibody molecule.

86. (New) A method according to claim 85, wherein the antibody is subjected to a protease digest to for Fab or F(ab')₂ fragments.